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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LE, EMILY M	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 06/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/978,423	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Emily Le	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04/12/2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *04/12/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/11/05 has been entered.

Status of Claims

2. Claims 1-57 and 63 are cancelled. Claims 58-62 are pending and under examination.

Correction of Inventorship

3. The request for the deletion of inventors in this nonprovisional application under 37 CFR 1.48(b) is deficient because:

i) An oath or declaration by each actual inventor or inventors listing the entire inventive entity has not been submitted.

ii) The statement of facts by an inventor or inventors to be added or deleted does not explicitly state that the inventorship error occurred without deceptive intent on his or her part or cannot be construed to so state.

iii) It lacks the required fee under 37 CFR 1.17(i). And/or

iv) It lacks the written consent of any assignee of one of the originally named inventors.

Information Disclosure Statement

4. The information disclosure statement filed 04/11/2005, Supplemental Information Disclosure Statement Under 37 C.F.R § 1.97 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the filling is incomplete. The statement filed is not accompanied with a listing of the document(s) on a PTO-1449, as set forth in 37 C.F.R § 1.98. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

5. The information disclosure statement (IDS) submitted 04/11/2005, under 37 C.F.R. § 1.97 has been considered by the Examiner. However, since the Blast results cited therein are not true publications with a publication date, they are not fully in compliance with 37 CFR 1.97 and thus they will not be printed on the face of the patent issuing from this application.

Claim Rejections - 35 USC § 101

6. Claims 58-62 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility.

In response to the rejection set forth in the previous office action, Applicant

submits the following, items i)-ii):

i) Applicant relies on the identification of the PRO701 protein as a neuroligin based on homology data for utility. This utility was first disclosed in U.S. Provisional No. 60/080328, filed 04/01/1998; which discloses:

"Beta neurexins and neuroligins are plasma membrane proteins that are displayed on the neuronal surface. Neuroligin 1 is enriched in synaptic plasma membranes and act as a splice site-specific ligand for beta neurexins as described by Ichtchenko et al. The extracellular sequence of neuroligin 1 is composed of a catalytically inactive esterase domain homologous to acetylcholinesterase. Neuroligin 2 and 3 are similar in structure and sequence to neuroligin 1. All neuroligins contain an N-terminal hydrophobic sequence with the characteristics of a cleaved single transmembrane followed by a large esterase homology domain, a highly conserved single transmembrane region and a short cytoplasmic domain. The three neuroligins are alternatively spliced at the same position and are expressed at high levels only in the brain. Tight binding of the three neuroligins to beta neurexins is observed only for beta neurexins lacking an insert in splice site 4. Thus, neuroligins constitute a multigene family of brain-specific proteins with distinct isoforms that may have overlapping functioning in mediating recognition processes between neurons. Moreover, neurexins and neuroligins have been reported as adhesion molecules in a Ca2+ dependent reaction that is regulated by alternative splicing of beta neurexins."

There are a number of papers that were published prior to Applicant's priority document which set forth the function of neuroligins in general. For example, Ichtchenko et al. teaches that subcellular fractionation of brain demonstrated that neuroligin 1 is enriched in synaptosomes similar to the post synaptic density protein PSD95, copurified with PSD95 on synaptic plasma membranes; suggests that the surface expression of neuroligin 1 and beta-neurexins on neurons leads to tight interactions between the organization of the synapse, thereby, increasing the specificity of the interactions or specifying a defined sequence of interactions; and indicate that neuroligins mediate cell-cell interactions between neurons. Nguyen and Sudhof discuss the binding properties of neuroligin 1 and neurexins 1 reveal that these molecules

function as hydrophilic cell adhesion molecules for mediating cell recognition between neurons. They also indicate that esterase-like domain is involved in binding the neurexins. Nguyen and Sudhof state that the binding of neurexins and neuroligins forms the nucleus for an intercellular junction. Finally, Irie et al. indicates that the extracellular domain of neuroligins 1, 2 and 3 tightly bind to the extracellular domain of neurexins. Thus, clearly it was known in the art at the time Applicants filed their provisional application that neuroligins were involved in mediating cell-cell recognition between nerve cells, likely at the synapses. Applicant identified a novel neuroligin with these properties.

Applicant's submission has been considered, however, it is not found persuasive. To provide clarification, the claimed invention is directed to any antibody that binds to SEQ IDNO: 375. In the instant, the utility for the antibody solely depends on the utility for the polypeptide. Ergo, both the Office and Applicant provide a utility analysis for the polypeptide.

It has been noted that Applicant discloses that the protein to which the claimed invention binds have homology (unspecified percentage) to neuroligins; however, mere identification that a protein belongs to a family of proteins, while indicative of evolutionary relatedness, is not indicative of function, nor by extension, of utility. In the instant, Applicant has not disclosed of a specific and substantial utility for the claimed invention.

A "specific utility" is specific to the subject matter claimed. This contrasts with a general utility that would be applicable to the broad class of the invention. In the instant,

Applicant has not provided a specific utility for the claimed invention. It is only noted that Applicant provided a general utility that would be applicable to the broad class of the invention, where Applicant asserts that the claimed invention can be employed for therapeutic purposes. In the instant, Applicant didn't identify the specific disease or condition that the claimed composition is capable of providing therapeutic properties against. Applicant has not identified with specificity why it is that the claimed invention is considered useful for therapeutic purposes. The expectation that the claimed invention can mediate cell-cell recognition between neurons and act as adhesion molecules in a Ca2+ dependent reaction is not sufficient to establish a utility for the claimed invention. What is the specific utility for a claimed invention that can mediate cell-cell recognition between neurons? Furthermore, what is the specific utility for a claimed invention that can act as adhesion molecules in a Ca2+ dependent reaction? A generic assertion of "for therapeutic purposes" is not sufficient to provide a specific utility for the claimed invention for the assertion is nonspecific to a disorder. Furthermore, just because the claimed invention may be deemed to have "useful biological" activities, such as cell-cell recognition and act as adhesion molecules in a Ca2+ dependent reaction, the identified useful biological activities are not sufficient to define a specific utility for the claimed invention.

This is further exemplified by the teaching of MPEP 2107.01, which states that the identification that a compound may be useful in treating unspecified disorders, or that the compound has "useful biological" properties, would not be sufficient to define a specific utility for the compound. Similarly, a claim to a polynucleotide whose use is

disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be specific in the absence of a disclosure of a specific DNA target. A general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what condition can be diagnosed. Contrast the situation where an applicant discloses a specific biological activity and reasonably correlates that activity to a disease condition. Assertions falling within the latter category are sufficient to identify a specific utility for the invention. Assertions that fall in the former category are insufficient to define a specific utility for the invention, especially if the assertion takes the form of a general statement that makes it clear that a "useful" invention may arise from what has been disclosed by the applicant. Knapp v. Anderson, 477 F.2d 588, 177 USPQ 688 (CCPA 1973). In the instant, Applicant's disclosure purely contains assertions that fall in the former category. The disclosure is replete with assertions that take the form of a general statement that alleges that based on homology to a genus of known protein, the claimed invention is expected to have similar activities as those expected of the genus;. thus, a "useful" invention may arise from what has been disclosed by Applicant. However, Applicant has not disclosed the context in which the claimed invention would be useful in a specific manner. Ergo, the asserted utility is not a specific utility.

A "substantial utility" defines a "real world" use. In the instant, Applicant has not defined a real world use for the claimed invention. MPEP § 2107.01 notes that a method of treating an unspecified disease or condition is an asserted utility that require or constitute carrying out further research to identify or reasonably confirm a "real world"

context of use and, therefore, do not define "substantial utilities".

In the instant, Applicant asserts that based on sequence homology to the neuroligin family, the claimed invention may be employed for therapeutic purposes. Such asserted utility is not substantial for the assertion does not specify the specific disease or condition that the claimed invention can be used to treat. Additionally, such asserted utility would require and constitute carrying out further research to identify or reasonably confirm a "real world" context of use. The same analysis applies should Applicant argues that the claimed invention have utility in mediating cell-cell recognition between neurons. This asserted utility is not substantial because there does not exist a real-world use for the asserted utility. Furthermore, the asserted utility would require and constitute carrying out further research to identify or reasonably confirm a "real world" context of use.

ii) Claims 58-62 also rely on the RAT DRG neuronal survival inhibition assay, Assay #58 for patentably utility for the PRO701 gene and the PRO701 protein and antibodies. This assay first disclosed in PCT/US00/04341 and U.S.S.N 09/918585, July 30, 2001. DRG neuronal survival assay is well recognized it the art and well used assay for measuring compounds which affect the growth of neural cells. Applicant notes that the in vitro sensory ganglia survival and outgrowth assays were used by Levi-Montalcini to identify Nerve Growth Factor. Applicant also noted that both Lewis et al. and Memberg et al. use the DRG survival assay for their analysis. Memberg indicates that proliferation in culture of DRG neuroblasts is consistent with in vivo data. Lewis et al. agrees that the assay is a recognized method of assaying for neurotrophic factors.

Thus, clearly, this assay is art recognized as being useful to identify compounds with various effects on neural development. If Applicant has asserted that the claimed invention is useful for any particular purpose and the assertion would be considered credible by any person of ordinary skill in the art. The logic underlying the asserted utility in the present case is not inconsistent with the general knowledge in the art, and would be considered credible by any person skilled in the art.

The remaining issue is whether there is sufficient nexus between in vitro data disclosed in the specification and the results a skilled artisan would expect in the treatment of neuropathies. "Nexus" requires a factually and legally sufficient connection between the objective evidence provided and the claimed invention, so that the evidence is of probative value in the determination of the issue that it is purported to support. There are peer-reviewed papers in the literature where the authors have used the DRG survival assay to identify neurotrophins and compounds which inhibit neuronal growth. The Examiner admits that the assay has been used to study the effects of various factors on neural development. Finally, this assay or one similar to it was used in the identification of Nerve Growth Factor, which is recognized as being a neurotrophin. Positive results with a drug candidate in a recognized in vitro assay have long been recognized by the Patent Office and competent courts as sufficient to support utility for claims covering compounds.

Applicant's submission has been considered, however, it is not found persuasive. MPEP § 2107.02 states that: An assertion is credible unless (A) the logic underlying the assertion is seriously flawed, or (B) the facts upon which the assertion is based are

inconsistent with the logic underlying the assertion. Credibility as used in this context refers to the reliability of the statement based on the logic and facts that are offered by the applicant to support the assertion of utility.

In the instant, Applicant is relying on a rat dorsal root ganglia (DRG) neuronal survival inhibition assay to provide a utility to the claimed invention. Applicant asserts that because the claimed invention tested positive in this assay, the claimed invention can be used for therapeutic treatment of neuropathic conditions which are associated with undesirable neural cell proliferation including neuroblastomas, gliomas, glioblastomas and the like.

Applicant's assertion in the specification has been extensively reviewed. While it is acknowledged that the assay is well established in the art; however, a search of the literature fails to reveal a correlation between compositions that tested in the assay and its use as a therapeutic agent of neuropathic conditions, including neuroblastomas, gliomas, glioblastomas and the like. Furthermore, there are no known exemplifications where this assay has been shown to correlate with therapeutic benefit such conditions/diseases, as exemplified by Memberg et al. and Lewis et al.

As noted by Applicant, the most that the art teaches is the use of the assay to identify compounds with various effects on neural development. However, the identification of compounds having various effects on neural development does not equate to it having a therapeutic purpose. To equate the noted effects to a therapeutic purpose, support must be provided, based on facts and logic. In the instant, Applicant asserts that because claimed composition has various effects on neural development;

ergo, the claimed invention have a therapeutic purpose for neuropathic conditions. However, Applicant did not substantiate the assertion with any facts or logic. As noted above, a search of the literature fails to reveal a correlation between compositions that tested in the assay and its use as a therapeutic agent of neuropathic conditions, including neuroblastomas, gliomas, glioblastomas and the like. Ergo, it is the facts and logic behind Applicant's asserted utility that are flawed. Nowhere in Applicant's submission or disclosure has Applicant offered any facts or logic to support Applicant's grand assertion of utility for the claimed invention, therapeutic purpose for neuropathic conditions.

Furthermore, it is unclear how the claimed invention can be used as a therapeutic agent of neuropathic conditions when the art teaches that the protein to which the claimed invention binds is also expressed in areas that are outside the brain, see Bolliger et al. Bolliger et al. teaches that the mRNA of the protein in which the claimed antibody binds, known in the art as neuroligin 4, has the highest relative expression in heart; and lower expression in liver, skeletal muscle and pancreas. Bolliger et al. also teaches that neuroligin 4 mRNA was hardly detectable in the brain, placenta, lung and kidney. With a low relevance in expression in the brain, it is unclear how the claimed invention could be use as a therapeutic agent of neuropathic conditions. Thus, Applicant's asserted utility is considered as incredible for it is not substantiated by any facts or logic. Applicant's assertion actually goes against logic and facts that exist in the art, as evidenced by the cited Bollinger et al., Memberg et al., Lewis et al., and Oppenheim et al.

Regarding Applicant's assertion that positive results with a drug candidate in a recognized in vitro assay have long been recognized by the Patent Office and competent courts as sufficient to support utility for claims covering compounds; Applicant is reminded that each application is treated on it's own merit, not the merit of other applications. In the instant, had Applicant relied on a reliable assay, one that provides a correlation between a composition and a therapeutic effect; then, Applicant's invention would most likely to have a credible utility. However, such correlation is absent for the assay Applicant used and the utility Applicant asserted.

Furthermore, as noted in the previous office action, the cell cultures Applicant used are a mixed population derived from embryonic neural tissue. Such are not necessarily representative of adult neural cells and tumor cells, as exemplified by the teaching in the art. Oppenheim et al. teaches that sensory neurons undergo substantial programmed cell death during early embryonic development. Lewis et al. teaches that factors that cause neonatal cell death such as peripheral nerve injury, growth factor withdrawal, ionization radiation, capsaicin, and sindbis virus infection do not have the same affect on adult neural cells. Adult neural cells are more resistant to these factors. Additionally, Memberg et al. teaches that the survival of neural cells depends on specific factors and the dependence changes with the age of the neural cells. Thus, due to the various known factors that are associated with embryonic neural tissues and how said tissues are different from adult neural, the results from Applicant's assay cannot be construed as a reliable. Thus, it is concluded that Applicant's asserted utility is not credible.

Additionally, it is noted that Applicant indicated that a copy of Levi-Montalcini was previously provided to the Office, such document cannot be located in the file nor is it found to be mentioned on any of the IDS(s) Applicant submitted. Should consideration of the document is desired, Applicant is requested to file an IDS, listing the identified document. Without the complete Levi-Montalcini disclosure, the Office cannot consider any arguments that Applicant submits using the teaching of the Levi-Montalcini disclosure. Ergo, any such submission would be considered moot and have no merit.

7. Claims 58-62 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial or credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Priority

8. In response to the rejection set forth above, Applicant submits the following: Applicant maintains that the subject matter define din claims 58-62 is emitted to the priority date of 04/01/1998, the filing date of Provisional Patent Application Serial No. 60/080328. At page 21, lines 4-7 of the provisional application, Applicant indicate that the PRO701 polypeptides of the invention possess the biological activity related to that of the neuroligin family. On page 1, lines 9-25, Applicant indicates that neuroligins constitute a multigene family of brain specific proteins with distinct isoforms that have overlapping functions in mediating recognition between neurons. Moreover, neurexins and neuroligins have been reported as functioning as adhesion molecules in a CA2+ dependent reaction that is regulated by alternative splicing of beta neurexins. In serial

No. 60/080328, Applicant references Ichtchenko et al., and Nguyen and Sudhof as references which describe the function of other related neuroligins. Based on Applicant's disclosure in 60/080328, Applicant maintains that Applicant is entitled to priority to the filing date of 60/080328, April 01, 1998 for the stated claims. Applicant correctly identified the polypeptide and the utility of the PRO701 polypeptide. Later published works by others, Bollinger and Jamain have confirmed the sequence and utility of the PRO701 polypeptide described by Applicant in their priority document.

Applicant also maintains that the subject matter defined in claims 58-62 is also entitled to the priority date of 02/18/2000, International Patent Application No. PCT/US00/04341. At pages 396-370, Example 140 of the application, Applicant indicates that the PRO701 polypeptide of the invention possess the biological activity related to the inhibition of survival of neural cells in culture. Based on Applicant's disclosure in the application, Applicant maintains that Applicant is entitled to the priority of the filing date of 02/18/2000 for the cited claims.

Applicant's submission has been considered, however, it is not found persuasive. MPEP § 2107.1 states: A deficiency under 35 U.S.C. 101 also creates a deficiency under 35 U.S.C. 112, first paragraph. If the application fails as a matter of fact to satisfy 35 U.S.C. § 101, then the application also fails as a matter of law to enable one of ordinary skill in the art to use the invention under 35 U.S.C. § 112.

In the instant, the applications upon which priority is claimed fail to provide adequate support under 35 U.S.C 112 for the claimed invention. Specifically, since the instant specification fails to provide a disclosure meeting the requirements of 35 U.S.C.

§ § 101 and 112, first paragraph, the claim for priority to any parent application is denied. The instant filing date, **10/16/01**, is thus used for the purpose of applying prior art. For reason(s) as to why the claims fail to have a utility, see the discussion provided under the utility heading.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 58-62 under 35 U.S.C. 102(b) as being anticipated by Ichtchenko et al, ("Neuroligin 1: A Splice Site-Specific Ligand for β–Neurexins", 1995) is maintained.

Applicant submits that claims 58-62 are directed at an antibody that "specifically binds" to SEQ IDNO: 375. Applicant submits that the term "specific binding" recited in the claims refer to an antibody that binds to a particular antigen without binding to another antigen. Therefore, the claims clearly refer to an antibody that is able to bind to the PRO701 polypeptide without cross-reacting with another antigen, including the sequences disclosed Ichtchenko et al. In view of this, the Examiner errs in assuming that the antibodies claimed in the presented application would bind to the polypeptide of Ichtchenko et al. While the amino acid sequence of neuroligin 1 taught by Ichtchenko et al. has some similarity to the PRO701 sequence, there are many different amino acid residues throughout the length of the sequences. As a result of the requirement of specific binding, the claims pending do not encompass antibodies that bind to the

polypeptide of Ichtchenko et al. As the Examiner is well aware, an antibody generally recognizes only a small region on the surface of the large molecule and the structure recognized by an antibody is called an epitope. The structures generally recognized by the antibody are located on the surface of the protein and such sites are likely to be composed of amino acids from different parts of the polypeptide chain that have been brought together by protein folding. Epitopes of this kind are known as conformational or discontinuous epitopes because the structure recognized is composed of segments of the protein that are discontinuous in the amino acid sequence of the antigen but are brought together in the three-dimensional structure. Most antibodies raised against intact, fully folded proteins recognized discontinuous epitopes. Secondly, the binding sites for the claimed antibodies cannot be simply be predicted based on linear sequence homology between the amino acid sequence of present invention and that of Ichtchenko et al. In view of the fact that most antibodies recognize discontinuous epitopes and not linear epitopes, it is even likely that an antibody will recognize and bind to linear fragments of a protein sequence.

Applicant's submission has been considered, however, it is not found persuasive. In the instant, Applicant's submission is not substantiated by any evidence showing that the antibody of Ichtchenko et al. is not an antibody that is encompassed by the claimed invention. Ergo, in the absence of evidence, such as binding epitopes or the amino acid sequence of the claimed antibody, that proves that the claimed antibody is different from that of the antibody that Ichtchenko et al. teaches, the rejection stands. In the instant, Ichtchenko et al. teaches of antibody that binds to a neuroligin protein, Neuroligin 1.

The amino acid sequence of neuroligin 1 has some similarity to the PRO701 sequence, as acknowledged by Applicant. Specifically, Neuroligin 1 have 71.4% identity to Neuroligin 4, the protein that Applicant identify as SEQ ID NO: 375. Thus, in view of the teaching that is shared between the two proteins and the absence of evidence that would indicate otherwise, the antibody of Ichtchenko et al. would necessarily bind to the same protein in which the claimed invention binds for an antibody generally recognizes only a small region on the surface of the large molecule, wherein the structure recognized by an antibody is called an epitope.

In addition to above, it is noted that Applicant has submitted declarations under 37 C.F.R § 1.131. Applicant is reminded that the instant rejection is a 102(b) rejection, and that prior invention may not be established under 37 C.F.R. §1.1.31 when the rejection is based upon a statutory bar (102(b) and 102(d)). Ergo, Applicant's submission under 37 C.F.R § 1.131 is not sufficient to overcome the instant 102(b) rejection.

Conclusion

10. No claim is allowed.

11. In addition to the objection(s) and rejection(s) set forth above, the following issue is noted from Applicant's 04/11/05 submission:

At the 1st full paragraph, on page 6 of the submission, Applicant notes that PRO701, which Applicant identifies as SEQ ID NO: 375 is recognized in the art as neuroligin 4. However, a sequence search for neuroligin 4 does not render a sequence that is 100% identical to SEQ ID NO: 375. It is found that neuroligin 4, also known in

the art as KIAA1260 have 96.9% identity to SEQ ID NO: 375, see Nagase et al. reference. Neuroligin 4 and SEQ ID NO: 375 differ from one another in the following manner:

i) claimed SEQ ID NO: 375 contains extra amino acid at position no: 139-158. Those 20 extra amino acid residues do not exist in Neuroligin 4.

ii) Applicant's asserted that the signal peptide for SEQ IDNO: 375 is amino acid residues 1-24 of SEQ ID NO: 375; however, the art teaches that the signal peptide for neuroligin 4 is amino acid residues 1-41 of neuroligin 4.

iii) The first 20 amino acid residues of SEQ ID NO: 375 do not correspond with the first 20 amino acid residues of neuroligin 4.

12. All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Le whose telephone number is (571) 272 0903. The examiner can normally be reached on Monday - Friday, 8 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey S. Parkin, Ph.D.
Primary Patent Examiner
Art Unit 1648

E.Le